REMARKS

Claims 1-38 are pending in the application. Claims 1, 2, 10-12, 15, 16, 18, 20, and 26 have been amended, and new claims 27-38 have been added. Support for the amendments and new claims can be found in the specification at, e.g., page 2, lines 1-4; page 5, lines 6-12 and 21-28; page 7, lines 3-11; page 8, lines 28-30; page 10, line 8, to page 11, line 10; page 11, lines 27-30; and page 12, lines 1-5. These amendments add no new matter.

35 U.S.C. §112, Second Paragraph (Indefiniteness)

At page 2 of the Office Action, the Examiner rejected claims 1-17, 20-22, and 26 as allegedly indefinite.

Claim 1 was rejected as indefinite in its recitation of the phrase "to thereby isolate the fusion protein." According to the Examiner, the claim "is unclear because there is no indication of what this is isolated from." Claim 1 has been amended to clarify that the fusion protein is isolated "from the biological sample."

Claim 2 was rejected on the basis that "it is unclear as to where in the sequence of steps of claim 1, the further step of 'clearing' occurs." Claim 2 has been amended to require that the cleaving of the first amino acid sequence from the second amino acid sequence follows the isolation of the fusion protein from the biological sample.

Claims 10-12 were rejected as "unclear as to where in the sequence of steps in claim 1, the further step of 'immobilizing' occurs and as to how this immobilizing is operative in achieving the overall purpose of the method." Claims 10-12 have been amended to require that the isolation of the fusion protein from the biological sample comprises immobilizing the fusion protein on a solid phase surface. The immobilizing can occur either (i) at the moment that the second member of the specific binding pair binds to the fusion protein (in those embodiments where the second member is immobilized prior to binding the fusion protein), or (ii) after the

second member of the specific binding pair binds to the fusion protein (in those embodiments where the second member is immobilized after binding the fusion protein). Immobilizing the fusion protein contributes to the overall method in that it can be used to facilitate the washing of unbound material and purifying of the fusion protein prior to its administration to the second mammal (see specification at e.g., page 10, line 8. to page 11, line 2).

Claim 20 was rejected "as unclear as to whether the first or the second amino acid sequence, or both, that 'the antibody response' of claim 18 is directed against. It is also unclear how the 'first member of a specific binding pair" is operative in method of claim 18." Claim 20 has been amended to require that the antibody response is generated against the first amino acid sequence. The "first member of a specific binding pair" recited in claim 20 is operative in the method of claim 18 in those embodiments that entail the isolation of the fusion protein from the biological sample via the binding of the fusion protein to a second member of the specific binding pair.

Claims 16 and 26 were rejected as "unclear as to where, in sequence of steps of base claims 1 and 18, the step of 'removing a B-cell' occurs." Claims 16 and 26 have been amended to require that the step of removing a B lymphocyte from the second mammal occurs following the administration to the second mammal of the fusion protein or a portion thereof comprising the first amino acid sequence (claim 16) or the protein (claim 26).

In light of the claim amendments and the foregoing comments, applicants respectfully submit that the claims satisfy the definiteness requirement. Accordingly, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §112, First Paragraph (Enablement)

At pages 2-3 of the Office Action, the Examiner rejected claims 1-17 and 20-22 as allegedly not enabled. According to the Examiner,

> Applicant's method lacks enablement because the claims leave out an essential step.
>
> In claim 1, between the binding and the administering steps, applicant has failed to recite the essential step of dissociating/releasing the first member of the specific binding pair (sbp) from the second member of the specific binding pair. Note Lo et al. (5,726,044) teach (Example 4) that, when an IL-2 Fc – gamma 1 fusion protein (in which the Fc-gamma-1 portion serves a first sbp) is purified by binding to solid phase Protein A (which serves as the second sbp), the fusion protein must be dissociated and eluted from the solid phase Protein A.

Applicants traverse the rejection in view of the following comments.

Dissociating or releasing the first member of the specific binding pair from the second member of the specific binding pair is not an essential step of the claimed methods. Instead, the methods can be carried out, for example, by cleaving the first amino acid sequence from the second amino acid sequence following the isolation of the fusion protein from the biological sample (amended claim 2 requires such a cleavage step). In addition, in some embodiments the entire fusion protein can be administrated to the second mammal (i.e., without cleavage of the first amino acid sequence from the second amino acid sequence). In such embodiments the fusion protein need not necessarily be dissociated from the second member of the binding pair. An effective immune response can in some cases be generated against the first amino acid sequence by administering to the mammal the entire fusion protein, even if it remains bound to the second member of the binding pair. As detailed in the specification, the fusion protein need not be purified to homogeneity to be useful in the claimed methods (see specification at, e.g., page 11, lines 3-13 and lines 24-30). The fusion protein can be unpurified, partially purified, or purified to homogeneity.

The Examiner cited Example 4 of Lo et al., U.S. Patent No. 5,726,044 to support the assertion that the fusion protein must be dissociated from the second member of the specific binding pair in the practice of the claimed methods. Example 4 of Lo et al. describes the

purification (via binding and elution from Protein A Sepharose) and characterization of an "IL2 immunofusin" protein. Example 4 describes electrophoresis analysis and enzyme activity assays for the purified protein. However, and contrary to the Examiner's comments in the Office Action, nothing in Lo et al. would have suggested to the skilled artisan that a fusion protein *must be* dissociated and eluted from a binding partner in order to be operable (i.e., result in an antibody response against the first amino acid sequence) in the claimed methods. Instead, the skilled biologist would have understood that in some embodiments the fusion protein can remain bound to the second member of the specific binding pair and remain effective in generating an antibody response against the first amino acid sequence when administered to the mammal.

In light of these comments, applicants respectfully submit that the claimed methods do not lack an essential step and the skilled biologist, at the time of filing of the present application, could have carried out the claimed methods without undue experimentation and with a reasonable expectation of success. Accordingly, applicants request that the Examiner withdraw the rejection of claims 1-17 and 20-22.

35 U.S.C. §102(b)

At pages 4-5 of the Office Action, the Examiner rejected claims 18, 25, and 26 as allegedly anticipated by Reid, U.S. Patent No. 6,054,632. According to the Examiner,

> [t]he administering of a nucleic acid and expressing of the encoded protein in a first mammal corresponds to the construction of a transgenic animal expressing an allelic form of a protein. An isolated nucleic acid encoding an allelic form of the protein is administered to a zygote (see col. 9, line 46 – col. 10, line 10). Applicant's disclosure has not limited the life stage of the "first mammal" in any way; thus microinjection of DNA into a mammal at the zygote stage is encompassed by the claim.

Applicants traverse the rejection in view of the claim amendments and the following comments.

Independent claim 18 has been amended to require that the nucleic acid is administered to the first mammal intravenously, intramuscularly, intraarterially, intradermally, intraperitoneally, intranasally, or subcutaneously. Reid describes introducing DNA into a single cell (a zygote) by

microinjection. Reid does not describe introducing a nucleic acid into a mammal by any of the specific routes of administration recited in amended claim 18. The routes recited in the amended claim require that the nucleic acid be administered via vasculature or other anatomical features of a mammal that are not present in a zygote. Accordingly, the "administering" step of amended claim 18 does not encompass the microinjection of a zygote described by Reid.

In light of the claim amendments and the foregoing comments, applicants respectfully submit that Reid does not anticipate amended independent claim 18 or claims 25 and 26 that depend therefrom. Applicants request that the Examiner withdraw the rejection.

At pages 5-7 of the Office Action, the Examiner rejected claims 1, 3, 6, 8, 10, 11, 13, and 17-22 as allegedly anticipated by Nemazee, U.S. Patent No. 5,698,679. According to the Examiner,

> Nemazee teaches production of nucleic acids encoding fusion proteins, which comprise two segments – an immunoglobulin segment and an inserted (usually in the CDR1 of the L chain) antigenic/epitopic peptide segment. These correspond, respectively, to instant "second" and "first" segments. Such nucleic acid segments can be used to produce transgenic animals (col. 18, lines 1+). As noted supra instant claims do not limit the life stage of the "first mammal" and thus encompass administration to zygotes. The first step of instant claims 1 and 18 is shown by Nemazee.

Applicants traverse the rejection in view of the claim amendments and the following comments.

Independent claims 1 and 18 have been amended to require that the nucleic acid is administered to the first mammal intravenously, intramuscularly, intraarterially, intradermally, intraperitoneally, intranasally, or subcutaneously. Nemazee describes introducing DNA into a zygote by microinjection. Nemazee does not describe introducing a nucleic acid into a mammal by any of the specific routes of administration recited in amended claims 1 and 18. As detailed above with respect to Reid, the routes recited in the amended claims require the administration of the nucleic acid via vasculature or other anatomical features of a mammal that are not present in

a zygote. Accordingly, the "administering" steps of amended claims 1 and 18 do not encompass the zygote microinjection described by Nemazee.

In light of the claim amendments and the foregoing comments, applicants respectfully submit that Nemazee does not anticipate amended independent claim 1 or 18 or the claims that depend therefrom. Applicants request that the Examiner withdraw the rejection.

Conclusions

Applicant asks that all claims be allowed in view of the amendments to the claims and the remarks presented herein.

Enclosed is a Petition for One Month Extension of Time and a check for the Petition for Extension of Time fee and excess claims fees. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 13062-004001.

Respectfully submitted,

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